

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1999/M 229	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/09466	International filing date (day/month/year) 28 September 2000 (28.09.00)	Priority date (day/month/year) 28 September 1999 (28.09.99)
International Patent Classification (IPC) or national classification and IPC C07D 251/16		
Applicant AVENTIS CROPSCIENCE GMBH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet. <input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of <u>3</u> sheets.
3. This report contains indications relating to the following items: I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 26 April 2001 (26.04.01)	Date of completion of this report 19 December 2001 (19.12.2001)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP00/09466

I. Basis of the report

1. This report has been drawn on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

☐ the international application as originally filed.

☒ the description, pages 1-25, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. 1(in part), 2-8,9(in part), 10(in part), 11(in part), 12(in part), as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1(in part), 9(in part), 10(in part), 11(in part), 12(in part), filed with the letter of 06 November 2001 (06.11.2001),
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

See the supplemental sheet.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-12	YES
	Claims		NO
Inventive step (IS)	Claims	1-12	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO

2. Citations and explanations

SEE SEPARATE SHEET

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: BOXES I, IV and V

1. The present application concerns a three-step method (amination (a), isocyanate production (b) and coupling (c)) for preparing phenylsulfonyl ureas from sulfohalogenides, at least one of the steps (a), (b) or (c) being carried out according to one of the preferred variants (a1), (b1) or (c1), as well as the individual preferred steps of this method.

The amendments to the claims concern only the deletion in variant (b1) of the alternatively defined implementation of the method with the admixture of an amine base.

2. The following documents are mentioned:

D1: WO-A-92/13845
D2: US-A-4 849 010
D3: US-A-2 852 557
D4: WO-A-96/06826
D5: EP-A-0 046 626
D6: US-A-4 238 621.

3. Novelty

The claimed method, in which amination or coupling are carried out in a defined solvent mixture ((a1), (c1)), has not been previously described:

D1, D2 and D6 describe only reactions in (aprotic) solvents such as tetrahydrofuran (D1: amination), dichloromethane (D2: amination and coupling) or

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: BOXES I, IV and V

acetonitrile (D6: coupling), while D3 describes the possibility to use a solvent mixture for amination, but not the specifically defined mixtures for the defined reaction.

D5 and D6 already describe the preparation of isocyanates, as defined in point (b1) in the claims, but with the admixture of an amine base.

D4 describes the production of isocyanates without the admixture of an amine base; however, these are isocyanates which do not bear a corresponding halogen for "X*".

The subject matter of the claims should therefore be considered novel.

4. Inventive step

4.1 Step (a1)

D1 and D2 can be regarded as the closest prior art and use aprotic solvents instead of the mixture defined in the application. The prior art examples (see, in particular, D1, Example 6, and also D2, Example 6) show a considerably lower yield than the examples in the present application. The measure described in step (a1) is not an obvious solution to the problem of devising a process with an increased yield.

4.2 Step (b1)

D5 and D6 already describe the preparation of

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: BOXES I, IV and V

halogen-substituted phenylsulfonyl isocyanates by reacting corresponding phenylsulfonamides with phosgene. D6 expressly recommends the use of an amine base (see column 4, line 53), while D5 does not expressly recommend the use of an amine base but, according to the examples, cannot dispense with the use of an amine base. However, the present application surprisingly shows that an amine base can be dispensed with for effectively producing halogen-substituted phenylsulfonyl isocyanates (>90%) and thus offers a non-obvious solution to the problem of devising a simplified but effective method for producing the phenylsulfonyl isocyanates in question.

Although D2 (column 33, lines 41-45) states that similar phenylsulfonyl isocyanates can be produced with or without an amine base, it does not dispense with an amine base in the examples. In this respect, D4 describes in the examples an effective method for producing phenylsulfonyl isocyanates without using an amine base, but not for producing halogen-substituted phenylsulfonyl isocyanates. D2 and D4 thus do not give any indication that the use of an amine base, which is expressly recommended in the closest prior art (D6), can be dispensed with in order to effectively prepare the phenylsulfonyl isocyanates defined in the application.

4.3 Step (c1)

According to Example 7a of the present application,

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: BOXES I, IV and V

coupling can be carried out with extremely high effectiveness (>99%), even without the admixture of an amine, by using the solvent mixture defined in step (c1), while the use of pure xylol as solvent leads to considerably lower yields.

D1, D2 and D6 represent the prior art with regard to the coupling according to step (c1); those documents describe the use of aprotic solvents instead of a particular solvent mixture. Although the examples in those documents cannot be directly compared with the example in the present application, it must be noted that the yields obtained in the prior art are considerably lower than the yields obtained according to the application (see D2 and D6). In this respect, the use of the defined solvent mixture must be assumed to represent an improvement. This improvement was not obvious to a person skilled in the art.

5. Unity of invention

Documents WO-A-92/13845 (D1) and US-A-4 849 010 (D2) already describe the preparation of phenylsulfonyl ureas (I), starting from sulfohalogenides (II) and passing by sulfonylamides (III) and sulfonyl isocyanates (IV) (see D1: page 7 and the examples; D2: Examples 6-8 and 13-15).

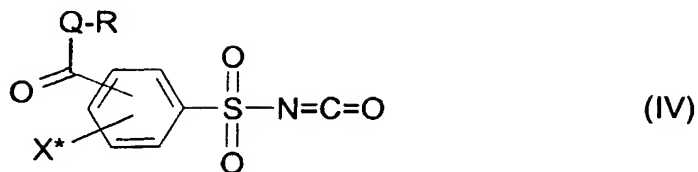
In relation to this prior art, the present application defines in the partial steps (a1), (b1) and (c1) advantageous modifications of the known

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: BOXES I, IV and V

transformations of II into III (a1), III into IV (b1) and IV into I (c1). However, these partial steps (a1), (b1) and (c1) are not linked by a common technical context from which a general inventive concept could be derived to substantiate unity of invention.

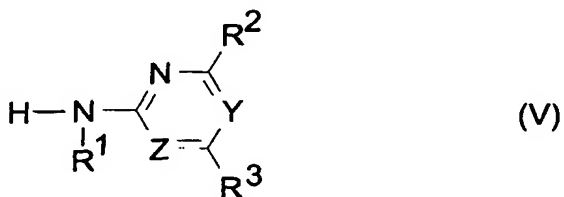


worin R, Q und X* wie in Formel (I) definiert sind,

oder vorzugsweise

(b1) im Falle X* = Halogen die erhaltene Verbindung (III) mit oder ohne Zwischenisolierung mit Phosgen zum Phenylsulfonylisocyanat der Formel (IV) umgesetzt und dabei die Umsetzung mit Phosgen in einem organischen Lösungsmittel in Gegenwart eines Isocyanats der Formel R'-NCO als Katalysator, wobei R' ein Kohlenwasserstoffrest ist, der unsubstituiert oder substituiert ist, oder eines Gemisches mehrerer dieser Isocyanate als Katalysator ohne Zugabe einer Aminbase durchführt,

- (c) die erhaltene Verbindung (IV) mit oder ohne Zwischenisolierung in einem organischen Lösungsmittel mit einem Amin der Formel (V)



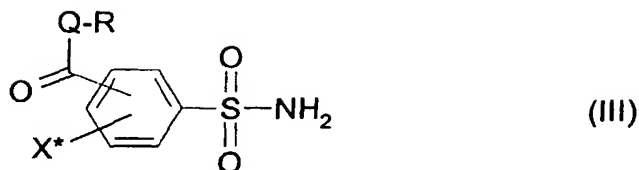
worin R¹, R², Y und Z wie in Formel (I) definiert sind,

zum Sulfonylharnstoff der Formel (I) oder dessen Salzen umgesetzt,

oder vorzugsweise

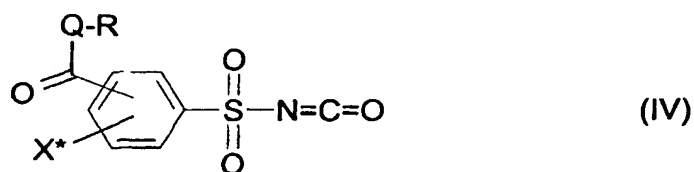
(c1) die erhaltene Verbindung (IV) mit oder ohne Zwischenisolierung in einem organischen Lösungsmittel mit einem Amin der Formel (V) zur

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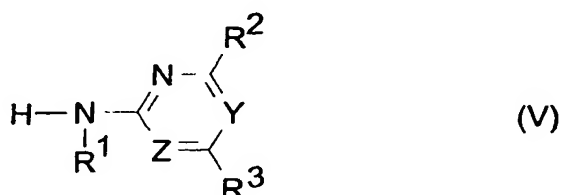
worin R, Q und X* wie in Formel (II) definiert sind,
mit Phosgen in einem organischen Lösungsmittel in Gegenwart eines oder mehrerer Isocyanate der Formel R'-NCO als Katalysator, wobei R' ein Kohlenwasserstoffrest ist, der unsubstituiert oder substituiert ist, ohne Zugabe einer Aminbase oder anderen Base als Ko-katalysator zum Phenylsulfonylisocyanat der Formel (IV) umgesetzt.

10. Verfahren zur Herstellung von Verbindungen der Formel (I) oder deren Salzen, wie sie nach einem der Ansprüche 1 bis 3 definiert sind, dadurch gekennzeichnet, dass man eine Verbindung der Formel (IV),



worin R, Q und X* wie in Formel (I) definiert sind,

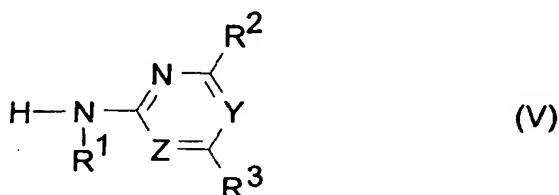
mit einem Amin der Formel (V)



worin R¹, R², Y und Z wie in Formel (I) definiert sind,

Gemisches mehrerer dieser Isocyanate als Katalysator ohne Zugabe einer Aminbase durchführt,

- (c) die erhaltene Verbindung (IV) mit oder ohne Zwischenisolierung in einem organischen Lösungsmittel mit einem Amin der Formel (V)



worin R^1 , R^2 , Y und Z wie in Formel (I) definiert sind,
zum Sulfonylharnstoff der Formel (I) oder dessen Salzen umsetzt,

oder vorzugsweise

(c1) die erhaltene Verbindung (IV) mit oder ohne Zwischenisolierung in einem organischen Lösungsmittel mit einem Amin der Formel (V) zur Verbindung der Formel (I) oder deren Salzen umsetzt und dabei die Umsetzung in einem Lösungsmittelgemisch aus einem gegebenenfalls halogenierten aromatischen Kohlenwasserstoff mit einem Siedepunkt von mehr als 110 °C und einem polaren aprotischen Lösungsmittel durchführt,

wobei im Verfahren mindestens einer der bevorzugten Teilschritte (b1) und (c1) durchgeführt wird.

12. Verfahren nach einem der Ansprüche 1 bis 11, dadurch gekennzeichnet, dass am Phenylring

- die Gruppe -CO-Q-R in Orthostellung zur substituierten Sulfonylgruppe steht,
- die Gruppe X^* = Halogen in Parastellung zur Gruppe -CO-Q-R steht und
- X = Halogen, vorzugsweise Iod bedeutet.